

Effect of Continuous Renal Replacement Therapy (CRRT) on Sepsis Induced Acute Kidney Injury (S-AKI) in Intensive Care Unit (ICU) Patients at Haji Adam Malik General Hospital Medan

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Abstract- Background: Sepsis AKI is associated with a higher risk of death and in-hospital mortality. Continuous Renal Replacement Therapy (CRRT) as the right choice in Sepsis AKI patients with hemodynamic instability, fluid overload.

Methods and Materials: This study used a descriptive method from 2020 to 2022 which was taken from the medical records of Haji Adam Malik General Hospital Medan. This study used a total sampling technique to recruit Sepsis AKI patients who were given CRRT according to inclusion and exclusion. This descriptive analysis was used to determine the characteristics of the sample, namely age, sex, urea change value, creatinine change value, NLR value, length of stay and mortality.

Results: There were 28 research samples consisting of 17 (60.7%) men and 11 (39.3%), urea levels before CRRT 173.21 ± 66.47 and after CRRT 117.28 ± 50.51 with a value $p = 0.00$. Creatinine levels before CRRT and after CRRT obtained creatinine levels before CRRT 6.21 ± 4.73 and after CRRT 3.2 ± 2.11 with an p value of 0.00 . The average NLR value before the CRRT was 34.93 ± 30.49 and after the CRRT was 33.22 ± 14.74 with an p value of 0.754 .

Conclusion: There is an effect of CRRT on Sepsis AKI patients where there is a decrease in creatinine and urea levels which were carried out in the RSUP H. Adam Malik.

Index Terms- CRRT, Sepsis AKI, Urea, Creatinine, NLR

I. BACKGROUND

Acute Kidney Injury (AKI) is a serious complication that often occurs in critically ill patients. A meta-analysis of 154 studies involving more than 3,000,000 individuals stated that 1 in 5 adults worldwide experience AKI during hospitalization. The incidence of AKI in patients treated in the Intensive Care Unit (ICU) is around 20-50%. Data from a multinational prospective study conducted by the Acute Kidney Injury-Epidemiologic Prospective Investigation (AKI-EPI) showed that AKI occurred in more than half of ICU patients, amounting to 57.3% with a mortality rate of 26.9%.^{1,2}

Sepsis AKI is associated with a higher risk of death and in-hospital mortality. If AKI has an overall mortality rate of 45%, the sepsis mortality rate for AKI is much higher, which is more than 70%. Bagshaw, et al in their study found that the mortality rate of sepsis cases of AKI in the hospital and ICU had increased, respectively by 30% and 20%, besides that it was also stated that the severity of AKI had a positive correlation with the morbidity and mortality rates of ICU patients, where the higher the severity of AKI, the higher the mortality rate.^{1,3}

The successful dialysis of patients with AKI in 1946 by Wilhem Kolf reduced AKI mortality by 50% and revolutionized the way we manage AKI. Since then it has remained an indisputable fact that patients with AKI should receive RRT although controversies exist about the optimal time to start, the best modality, and the dose of dialysis to be administered to the patient.⁴

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Hemodialysis is usually used to treat sepsis by removing some harmful macromolecular substances, including inflammatory mediators in the body, thereby purifying the blood.⁵ In addition to hemodialysis, CRRT therapy is a treatment option for patients with Sepsis AKI.^{6,7} In several clinical studies, CRRT has been shown to be beneficial because it is better tolerated in patients with hemodynamic instability and has a better recovery effect on the kidney.⁸

II. METHOD

This study is an analytical study with a retrospective cohort study design. Retrospective cohort is a study that examines backwards using secondary data, to see whether there is a relationship between the independent variables and the dependent variable. The design of this study aims to determine the effect of continuous renal replacement therapy (CRRT) on AKI sepsis in ICU treated patients.

The study population was all patients diagnosed with AKI sepsis and being treated in the ICU for the period 2020 to 2022. The sample of this study was part of the study population that met the inclusion and exclusion criteria using the total sampling method of data collection.

The data collected in this study were secondary data obtained from the medical records of the study subjects, consisting of identity (gender, age), comorbidities, use of vasopressors, SOFA score, APACHE II score, EWS score, urea, creatinine, NLR, and length of stay.

III. RESULTS

This research is analytic in nature with a retrospective research method with secondary data sources obtained from medical record data at HAM Hospital for the period 2021 to 2022, with a sample of 28 medical records in this study.

Table 1 Sample Characteristics

Gender		N	%
	Man	17	61%
	Woman	11	39%
Age			
	18–26 years	2	7%
	27–35 years	3	11%
	36–44 years	1	4%
	45–53 years	4	14%
	54–62 years	5	18%
	63–72 years	13	46%
RIFLE			
	risk	7	25%
	injured	6	21%
	Failure	15	54%
	Loss of Function	0	0%
	EndStage	0	0%
Comorbid			
	DM	7	25%
	CAD	10	36%
	Hypertension	6	21%

	HIV	2	7%
	tuberculosis	1	4%
	Cancer	1	4%
	CHF	1	4%
FOLDER			
	<65	0	0%
	66-75	7	25%
	76-85	10	36%
	86-95	6	21%
	>96	5	18%
modifiedSOFA			
	0-6 (<2%)	0	0%
	7-9 (0-10%)	0	0%
	10-12 (10-30%)	8	29%
	13-14 (40-60%)	17	61%
	15 (75-90%)	3	11%
	16-24 (>90%)	0	0%
APACHE II			
	0-4 (4%)	0	0%
	5-9 (8%)	0	0%
	10-14 (15%)	1	4%
	15-19 (24%)	3	11%
	20-24 (40%)	1	4%
	25-29 (55%)	7	25%
	30-34 (73%)	6	21%
	>35 (85%)	10	36%
EWS			
	1-4 (Low)	7	25%
	5-6 (Medium)	6	21%
	□ □ □ Heavy □	15	54%
norepinephrine			
	<0.3	4	14%
	0.3-0.5	12	43%
	0.5-1.0	12	43%
Dobutamine			

0	24	84%
≤ 5	2	8%
6-10	1	4%
11-15	0	0%
16-20	1	4%

In Table 1, there are 17 (61%) males and 11 (39%) females.

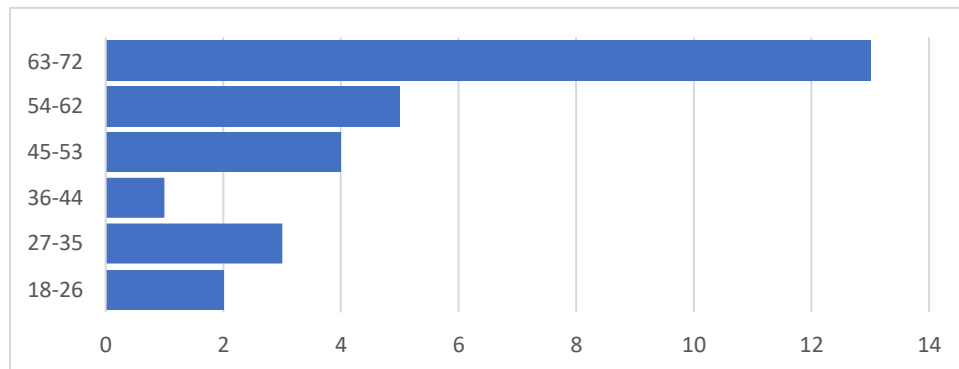


Figure 1 Sample Age Histogram

The sample distribution for the age group 18-26 years is 2 people (7%), for the age range 27-35 years is 3 people (11%), for the age range 36-44 years is 1 person (4%), the age range 45-53 years is 4 people (14%), for the 54-62 years there were 5 people (18%) and for more than 63-72 years there were 13 people (46%).

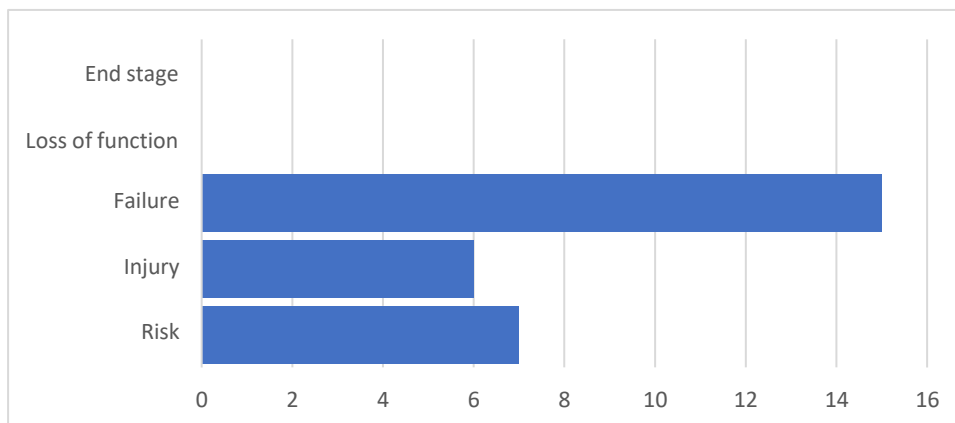


Figure 2 Sample RIFLE Classification Histogram

For RIFLE classification in this study, there were 7 people (25%) with risk stage, 6 people (21%) with injury stage and 15 people (54%) with failure stage.

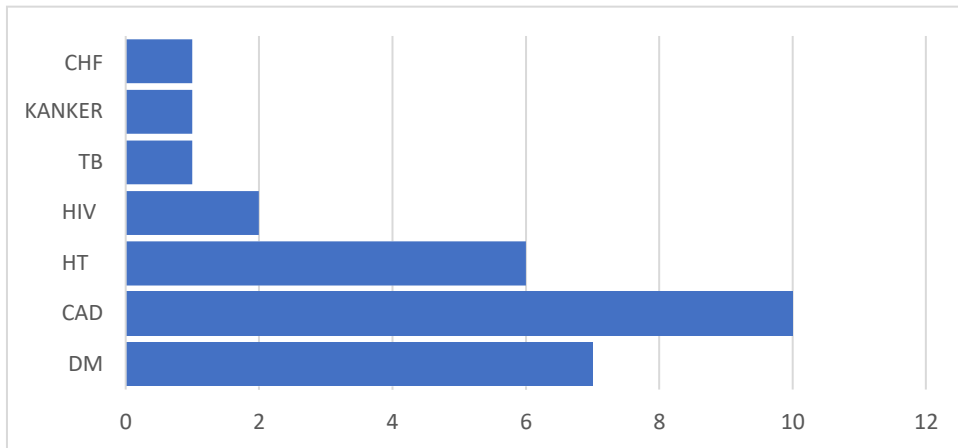


Figure 3 Sample Comorbid Histogram

From the sample comorbid data, there were 7 people (25%) DM comorbids, 10 people (36%) CAD, 6 people (21%) hypertension, 2 people (7%) HIV, 1 TB person (4%), cancer in 1 person (4%), and CHF in 1 person (4%).

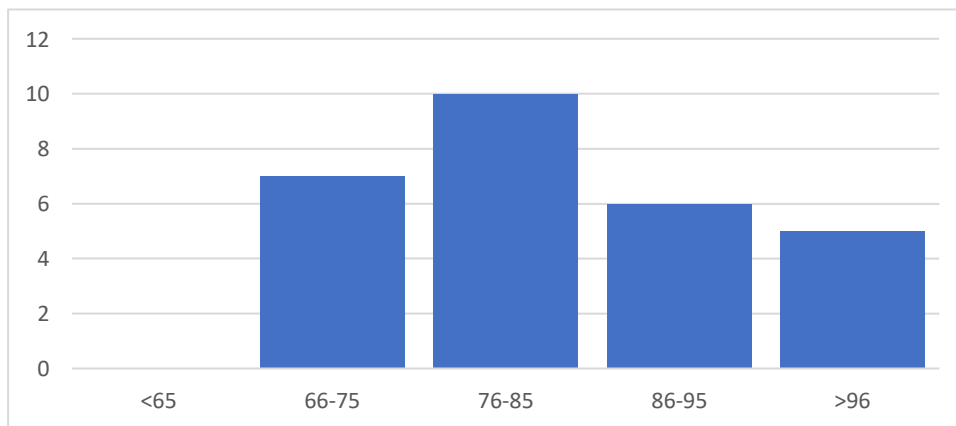


Figure 4 MAP Histogram

MAP characteristics of the samples at the initiation of CRRT, obtained MAP 66- 75mmHg in 7 people (25%), MAP 76-85mmHg in 10 people (36%), MAP 86-95mmHg in 6 people (21%), and MAP >96mmHg in 5 people (18%).

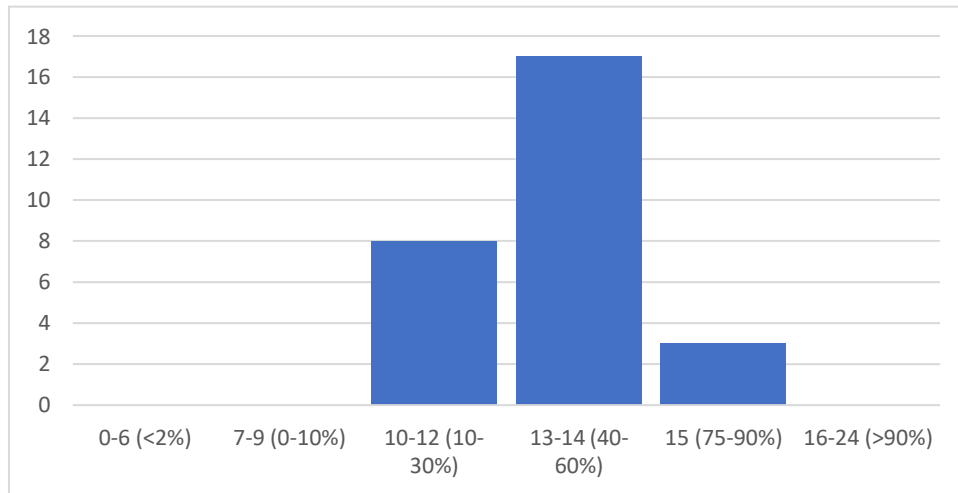


Figure 5 mSOFA Histogram

For the mSOFA score criteria, 8 people (29%) had SOFA scores of 10-12, mSOFA scores of 13-14 for 17 people (61%), and mSOFA scores of 15 for 3 people (11%).

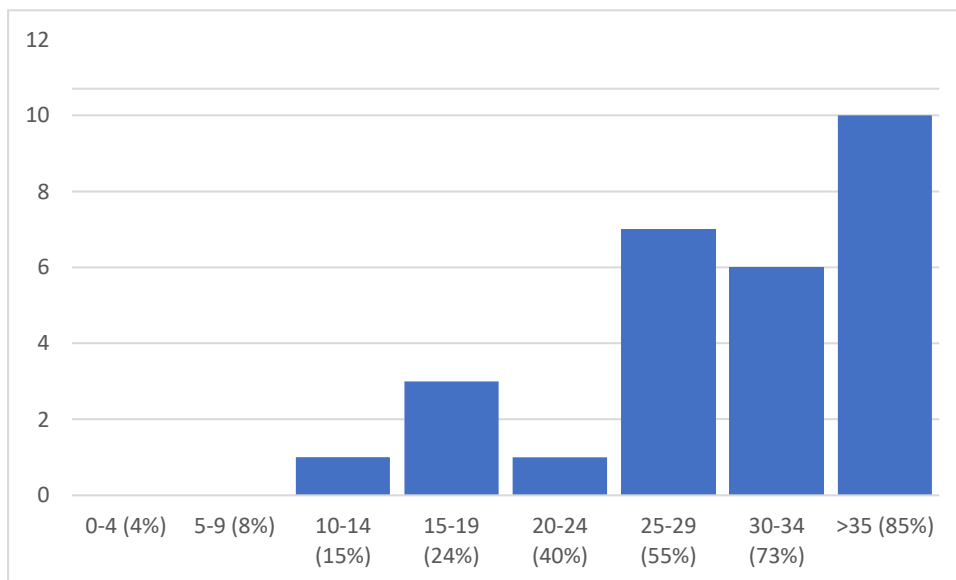


Figure 6 APACHE II Histogram

Characteristics of the APACHE II score found 1 person (4%) APACHE II score 10-14, 3 people (11%) APACHE II score 15-19, 1 person (4%) APACHE II score 20-24, APACHE II score 25-29 in 7 people (25%), APACHE II score of 30-34 in 6 people (21%), and APACHE II score > 35 in 10 people (36%).

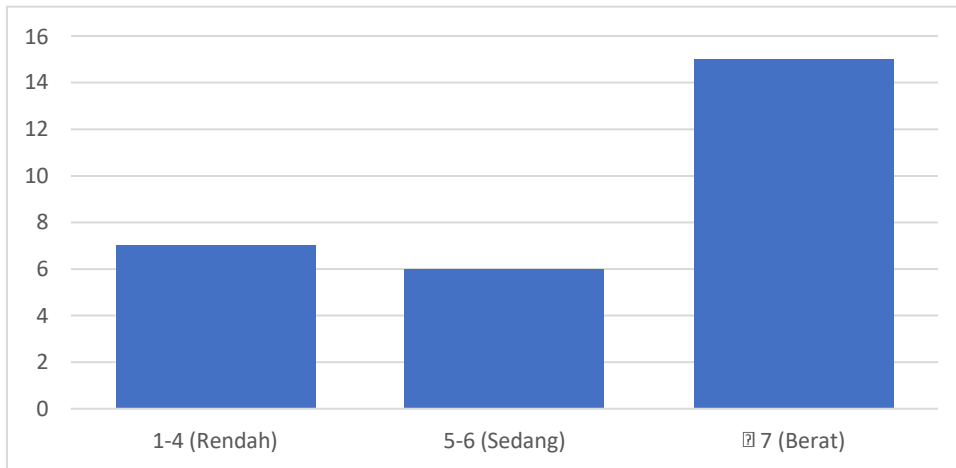


Figure 7 EWS Histograms

EWS scores 1-4 were 7 people (25%), EWS scores 5-6 were 6 people (21%), and EWS scores >7 were 15 people (54%).

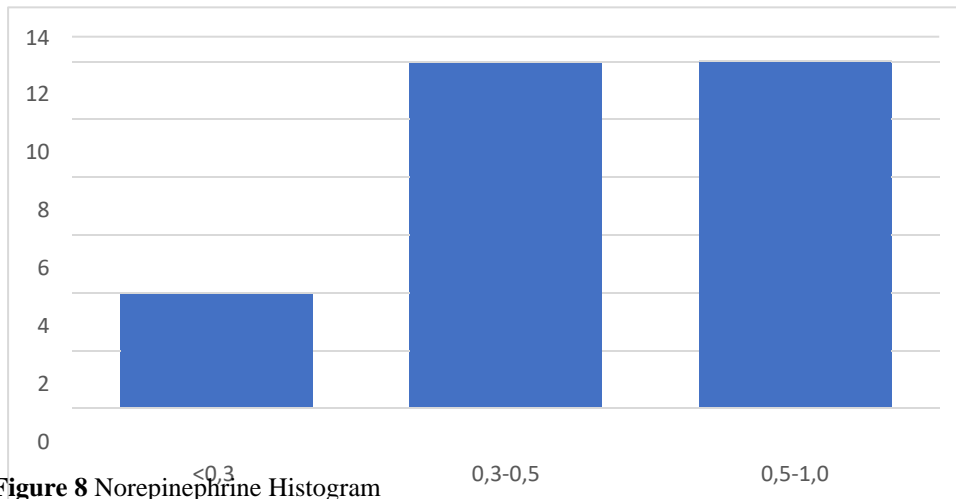


Figure 8 Norepinephrine Histogram

Use of vasopressors in the form of norepinephrine dose <0.3mcg/kg/min in 4 people (14%), norepinephrine dose 0.3-0.5mcg/kg/min in 12 people (43%), and norepinephrine dose 0.5-1mcg/kg/min in 12 people (43%).

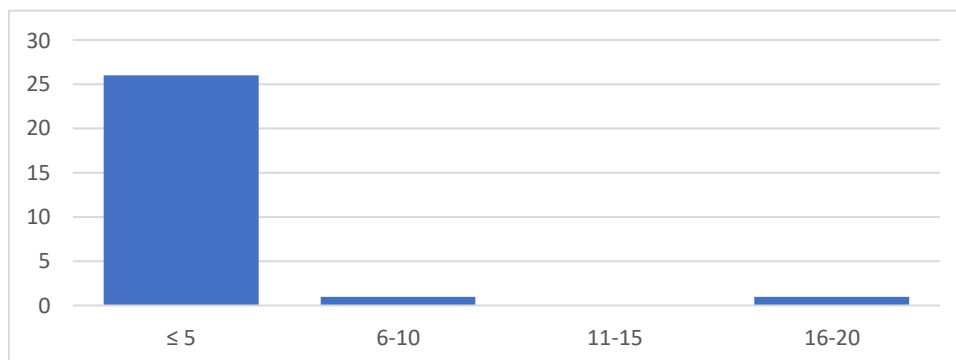


Figure 9 Dobutamine Histogram

Dobutamine <5mcg/kg/min was found in 2 (8%), 6-10mcg/kg/min in 1 (4%), 16-20mcg/kg/min in 1 (4%), and 24 people did not use dobutamine (84%).

Table 2 Sample Characteristic Normality Test

	Mean ± SD	p
Age	54.3214 ± 15.60877	0.001
FOLDER	83.4286 ± 12.84791	0.22
norepinephrine	0.4798 ± 0.21177	0.337
Dobutamine	1.1786 ± 3.42165	0.001
mSOFA	13.0714 ± 1.24510	0.054
APACHE II	31.0714 ± 8.26832	0.584
EWS	7.2145 ± 3.03507	0.038

*Shapiro-Wilk test

Normality test of the age is 54.3214 ± 15.60877 with a p value of 0.001, norepinephrine value was 0.4798 ± 0.21177 with a p value of 0.337, dobutamine value was 1.1786 ± 3.42165 with a p value of 0.001, mSOFA value was 13.0714 ± 1.24510 with a p value of 0.054, the APACHE II value was 31.0714 ± 8.26832 with a p value of 0.584 and the EWS value was 7.2145 ± 3.03507 with a p value of 0.038. So it can be concluded that norepinephrine, mSOFA, and APACHE II are significant to the sample characteristic normality test.

Table 3 Variable Normality Test

	Mean ± SD	p
Urea Pre	173.2143 ± 66.47269	0.547
Urea Post	117.2857 ± 50.51722	0.07
Creatinine Pre	6.2121 ± 4.73659	0.001
Creatinine Post	3.2250 ± 2.18694	0.002
NLR Pre	34.9289 ± 30.48041	0.001
NLR Post	33.2207 ± 14.74063	0.211

*Shapiro-Wilk test

The mean of pre urea value is 173.2143 ± 66.47269 with a p value of 0.547, post urea value was 117.2857 ± 50.51722 with a p value of 0.07, pre creatinine value was 6.2121 ± 4.73659 with a p value of 0.01, creatinine value post was 3.2250 ± 2.18694 with a p value of 0.002, the pre NLR value was 34.9289 ± 30.48041 and the post NLR value was 33.2207 ± 14.74063 with a p value of 0.211, it can be concluded that the urea pre, urea post and NLR post significant to variable normality test.

Table 4 Changes in Urea Before CRRT and After CRRT

	Before	After	P*
Urea	173.21 ± 66.47	117.28 ± 50.51	0.001

*Pair T-Test

From the data table 4 changes in urea before CRRT and after CRRT, the urea value before CRRT was 173.21 ± 66.47 and after CRRT 117.28 ± 50.51 with a p value of 0.001, so it can be concluded that there was a significant change between the urea value before and after CRRT.

Table 5 Changes in Creatinine Before CRRT and After CRRT

	Before	After	P*
Creatinine	6.21 ± 4.73	3.2 ± 2.11	0.007

* Wilcoxon Signed Ranks Test

From the data table 5, the creatinine value before CRRT and after CRRT obtained the creatinine value before CRRT 6.21 ± 4.73 and after CRRT 3.2 ± 2.11 with a p value of 0.007,

it can be concluded that there was a significant change between the creatinine value before and after CRRT.

Table 6 NLR Changes Before CRRT And After CRRT

	Before	After	P*
NLR	34.93 ± 30.49	33.22 ± 14.74	0.785

* Wilcoxon Signed Ranks Test

Based on table 6 the change in the NLR value before the CRRT was 34.93 ± 30.49 and after the CRRT was 33.22 ± 14.74 with a p value of 0.785 > 0.05, there was no significant change between the NLR values before and after CRRT.

Table 7 Length of Stay

	Mean ± SD
Length of Stay	3.46 ± 3.24

*Descriptive analytics

Based on table 7, the average length of stay was 3.46 ± 3.24 in sepsis AKI patients undergoing CRRT in the ICU of Haji Adam Malik General Hospital Medan.

DISCUSSION

Studies generally find sepsis in AKI to be associated with older age, greater comorbidities, nonsurgical disease, higher disease severity, greater deviation in hemodynamic parameters, greater need for mechanical ventilation and vasopressor support, intense inflammatory response, hematology, and acid-base homeostasis⁹⁻¹²

In this study, the urea value before CRRT was 173.21 ± 66.47 and after CRRT 117.28 ± 50.51 with a p value of 0.001. It can be concluded that there was a significant change between the average urea value before and after CRRT. This is consistent with a study conducted by Hideto et al (2014) where the urea value was 180 before CRRT and the urea value after CRRT was 177. In the study conducted by Li et al (2022), in which 16 people were diagnosed with sepsis AKI, a urea value of 516.5 was obtained before CRRT and a urea value after CRRT was 352.2.13 According to the KDIGO (Kidney Disease Improving Global Outcomes) Clinical Practice Guideline, CRRT is recommended for patients with impaired kidney function, where there is an increase in the value of urea and creatinine levels which aims to control the uremic state.¹³

In this study, the creatinine value before CRRT was 6.21 ± 4.73 and after CRRT was 3.2 ± 2.11 with a p value of 0.007. So it can be concluded that there is a significant change between the creatinine value before and after CRRT. This is in accordance with previous research, where 16 people diagnosed with AKI sepsis, obtained a mean creatinine value before CRRT was 25.7 and after CRRT creatinine value was 24.25.70 In another study, the average value before CRRT was 2.80 and after CRRT of 1.56 with a p value of 0.001, there is a significant relationship between the decreasing variables.¹⁴

In sepsis AKI patients in the ICU of Haji Adam Malik Hospital, the majority of patients experienced a decrease in absolute lymphocyte levels accompanied by an increase in absolute neutrophil levels so that NLR levels were quite high in sepsis patients in the ICU of Haji Adam Malik Hospital. NLR can be a cheaper and easier alternative as a biomarker of inflammatory reactions compared to C-reactive protein and cytokines such as IL-6. In this study, the NLR value before the CRRT was 34.93 ± 30.49 and after CRRT was 33.22 ± 14.74 with a p value of 0.785 > 0.05 which means there was a decrease in NLR, but there was no significant change between NLR before and after CRRT. This is in accordance with a study conducted by Ela et al (2022) where CRRT was performed on 16 patient samples, the NLR value was obtained before CRRT was 30, 36 and after CRRT 26.01. There was a decrease in NLR levels but there was no significant change between the variables. In a study conducted by Wang et al (2022) in patients with AKI the value of NLR before CRRT was 11,86 and after CRRT was 11,11 with p value 0,56 which stated there is no significant difference between variables, although there was a decrease in NLR levels, it was not statistically significant.¹⁵ These results corroborate previous research so that it can be concluded that the function of NLR as an inflammatory marker to assess the effect of CRRT on sepsis AKI is still not good.

The length of stay after the patient underwent CRRT in this study was 3.46 days, this is the same as a study conducted by Yasuda et al where the length of stay of patients after CRRT was 3.34 days.¹⁶

IV. CONCLUSION

In this study, it was found that CRRT had a positive effect on sepsis AKI patients treated in the ICU of Haji Adam Malik Hospital, Medan, as assessed by urea, creatinine, and NLR. The patient's urea level after CRRT decreased where the urea level before CRRT was 173.21 ± 66.47 and after CRRT was 117.28 ± 50.51. The patient's creatinine level after CRRT decreased where the creatinine level

before CRRT was 6.21 ± 4.73 and after CRRT was 3.22 ± 2.11 . The NLR value before the CRRT was 34.93 ± 30.49 and after the CRRT was 33.22 ± 14.74 . The patient's length of stay after CRRT was 3.46 ± 3.24 days.

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